

The Reaction of 1,2,3-Triazines with Grignard Reagents

Akio Ohsawa, Terumitsu Kaihoh, and Hiroshi Igeta*

School of Pharmaceutical Sciences, Showa University, Tokyo 142, Japan

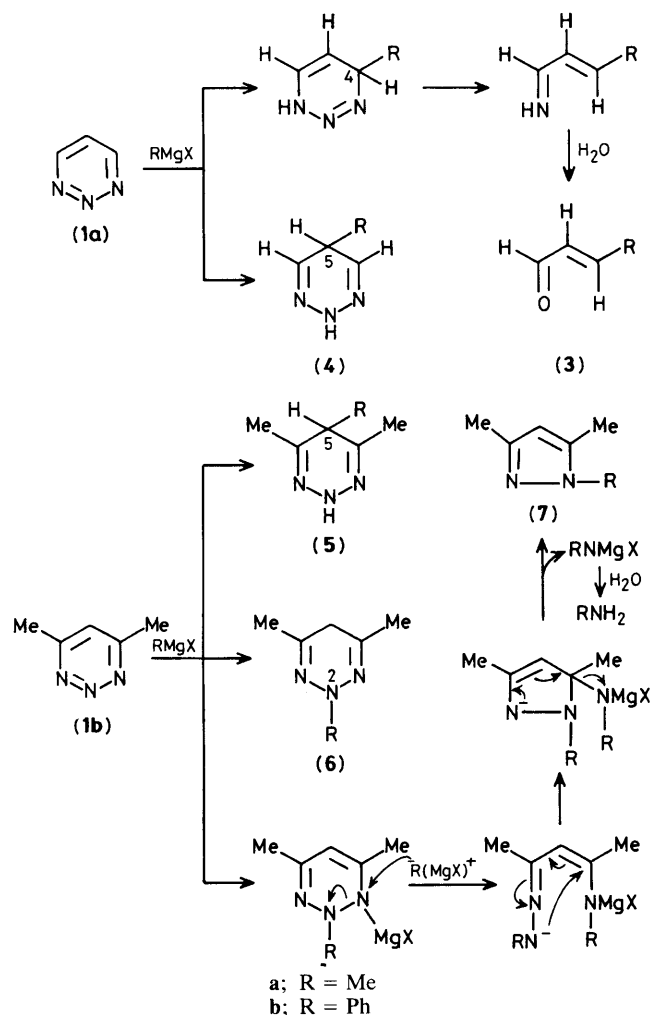
Monocyclic 1,2,3-triazines reacted with Grignard reagents to form adducts due to N-2 and C-5 attack together with β -substituted acrylaldehydes and *N*-substituted pyrazoles; the results show that the N-2, C-4, and C-5 positions are reactive towards Grignard reagents.

The behaviour of 1,2,3-triazines (**1a**) and (**1b**) towards Grignard reagents is noteworthy owing to their π -deficient character. With regard to this, the reactions of 4-substituted 1,2,3-benzotriazines (**2**) with alkyl Grignard reagents were demonstrated by Storr *et al.*¹ and it was found that attack by the reagents occurs at N-2. The reaction sites of (**2**), however, are quite restricted and the reactivity of the triazine ring might be influenced to some extent by the fused benzo moiety. This paper describes the reaction of monocyclic 1,2,3-triazines (**1a**) and (**1b**) with Grignard reagents.

1,2,3-Triazine (**1a**)² was treated with 1 equiv. MeMgI (in Et₂O, at 0 °C \rightarrow room temp. for 0.5 h) and then quenched with aq. NH₄Cl. The v.p.c.-mass spectrum of the ethereal layer† showed the presence of a reasonable amount of crotonaldehyde (**3a**),‡ but the major product was the symmetrical adduct, 5-methyl-2,5-dihydro-1,2,3-triazine (**4a**), (42%

† Ionization of the molecule was carried out at 70 eV; *m/z* 70, 100%; 69, 48%; 41, 87%; 39, 55%.

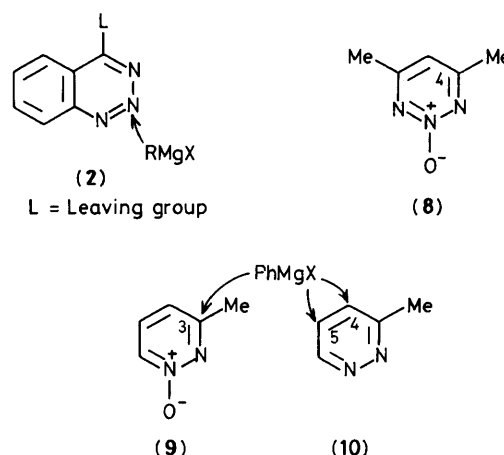
‡ Isolation of crotonaldehyde has not been accomplished.



Scheme 1

yield).§ Treatment of (**1a**) with PhMgBr under similar conditions and work-up gave cinnamaldehyde (**3b**) (52%) and the 2,5-adduct (**4b**) (13%).§

§ Compound (**4a**), colourless flakes (hexane– Et_2O), m.p. 53–55 °C, ^1H n.m.r. (CDCl_3) δ (vs. SiMe_4): 1.32 (3H, d, J 6.7 Hz, CHCH_3), 2.16 (1H, q, J 6.7 Hz, CHCH_3), 6.50 (2H, s, $\text{N}=\text{CH} \times 2$), 8.80 (1H, br. s, NH); ^{13}C n.m.r. (CDCl_3) δ (vs. SiMe_4): 13.45 (CH_3), 27.39 (CHCH_3), 139.98 ($\text{N}=\text{CH}$). (**4b**), colourless needles (hexane– Et_2O), m.p. 94–97 °C, ^1H n.m.r. δ : 3.18 (1H, br. d, J 1.5 Hz, CHPh), 6.61 (2H, d, J 1.5 Hz, $\text{N}=\text{CH} \times 2$), 7.10–5.0 (5H, m, phenyl), 8.82 (1H, br. s, NH); ^{13}C n.m.r. δ : 39.03 (CHPh), 127.72, 128.28, 129.06 (phenyl carbons), 133.18 ($\text{N}=\text{CH}$), 137.83 (phenyl 1-C). The adduct (**5a**) was identical with the compound which was obtained from 4,5,6-trimethyl-1,2,3-triazine by catalytic hydrogenation (Pd-C) or NaBH_4 reduction in MeOH ; colourless needles, (pentane– Et_2O), m.p. 52–54 °C, ^1H n.m.r. δ : 1.02 (3H, d, J 6.6 Hz, CHCH_3), 2.00 (6H, s, $\text{N}=\text{C}-\text{CH}_3 \times 2$), 2.67 (1H, q, J 6.6 Hz, CHCH_3), 8.45 (1H, br. s, NH). Compound (**6a**) was authentically obtained from NaBH_4 reduction (in MeOH) of 2,4,6-trimethyl-1,2,3-triazinium iodide; colourless oil, ^1H n.m.r. δ : 2.00 (6H, s, $\text{N}=\text{C}-\text{CH}_3 \times 2$), 2.38 (2H, s, CH_2), 3.30 (3H, s, NCH_3). (**5b**), colourless prisms (Et_2O), m.p. 109–111 °C, ^1H n.m.r. δ : 1.95 (6H, s, $\text{N}=\text{C}-\text{CH}_3 \times 2$), 3.75 (1H, s, CHPh), 6.90–7.22 (5H, m, phenyl), 8.08 (1H, br. s, NH); ^{13}C n.m.r. δ : 20.76 (CH_3), 44.35 (CHPh), 127.45, 128.03, 128.91 (phenyl carbons), 137.12 (phenyl 1-C), 141.17 ($\text{N}=\text{C}-\text{CH}_3$). (**6b**) pale yellowish prisms (Et_2O), m.p. 51–52 °C, ^1H n.m.r. δ : 2.09 (6H, s, $\text{N}=\text{C}-\text{CH}_3 \times 2$), 2.59 (2H, s, CH_2), 6.78–7.60 (5H, m, phenyl); ^{13}C n.m.r. δ : 21.90 (CH_3), 29.90 (CH_2), 115.54 (phenyl 3-C), 121.87 (phenyl 4-C), 128.55 (phenyl 2-C), 139.88 (phenyl 1-C), 147.52 ($\text{N}=\text{C}-\text{CH}_3$).



The formation of aldehydes (**3**) is the result of nucleophilic attack by the Grignard reagent at C-4 of the triazine (**1a**), and thus reveals that C-4 and C-5 of the triazine are reactive towards Grignard reagents.

In the case of triazine (**1b**),³ where both C-4 and C-6 are blocked with methyl groups, the reaction with MeMgI afforded the symmetrical adducts, 4,5,6-trimethyl-2,5-dihydro-1,2,3-triazine (**5a**) (20%)§ and 2,4,6-trimethyl-2,5-dihydro-1,2,3-triazine (**6a**) (25%),§ and *ca.* 10% of 1,3,5-trimethylpyrazole (**7a**). The reaction of (**1b**) with PhMgBr gave compound (**5b**) (6%),§ the dihydro compound (**6b**) (37%),§ and the pyrazole (**7b**) (10%). In addition, the presence of aniline in the reaction mixture was confirmed by v.p.c.

Of the products from (**1b**), the compounds (**5**) and (**6**) are the products caused by C-5 attack and N-2 attack, respectively, and the formation of compounds (**7**) might proceed *via* a sequence which involves attack at N-2 as shown in Scheme 1.¶

Thus, the data show that not only N-2 but also C-4 and C-5 of the 1,2,3-triazines are reactive towards Grignard reagents and this appears to be the first isolation of adducts owing to N-2 and C-5 attack on the 1,2,3-triazines by Grignard reagents.

Additionally, treatment of 4,6-dimethyl-1,2,3-triazine 2-oxide (**8**)^{3||} with the Grignard reagents under the conditions described resulted in almost complete recovery of the starting material, a rather unexpected result because C-3 of 3-methylpyridazine 1-oxide (**9**),⁴ which is positionally comparable with C-4 of compound (**8**), is reactive with PhMgBr under similar conditions, as are C-4 and C-5 of 3-methylpyridazine (**10**).⁵

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¶ Treating (**6a**) with MeMgI under the described conditions did not give (**7**); it resulted in essentially complete recovery of (**6**).

|| Details of nucleophilic reactions on the triazine *N*-oxides will appear later.